

We Claim:

1. A composition comprising a TNF- α binding molecule, or a nucleic acid sequence encoding a TNF- α binding molecule, wherein said TNF- α binding molecule comprises; i) a CDRL3 sequence comprising SEQ ID NO: 33, and ii) a CDRH3 comprising SEQ ID NO: 53.

5 2. The composition of Claim 1, wherein said TNF- α binding molecule further comprises iii) a CDRL1 sequence comprising SEQ ID NO: 15, and iv) a CDRL2 sequence comprising SEQ ID NO: 25.

10 3. The composition of Claim 2, wherein said TNF- α binding molecule further comprises v) a CDRH1 sequence comprising SEQ ID NO: 37, and vi) a CDRH2 sequence comprising SEQ ID NO: 45.

15 4. The composition of Claim 2, wherein said TNF- α binding molecule further comprises v) a CDRH1 sequence comprising SEQ ID NO: 39, and vi) a CDRH2 sequence comprising SEQ ID NO: 45.

20 5. The composition of Claim 1, wherein said TNF- α binding molecule further comprises iii) a CDRL1 sequence comprising SEQ ID NO: 13, and iv) a CDRL2 sequence comprising SEQ ID NO: 27.

25 6. The composition of Claim 5, wherein said TNF- α binding molecule further comprises v) a CDRH1 sequence comprising SEQ ID NO: 37, and vi) a CDRH2 sequence comprising SEQ ID NO: 55.

30 7. The composition of Claim 1, wherein said TNF- α binding molecule further comprises a light chain variable region, wherein said light chain variable region comprises a human germline framework region.

8. The composition of Claim 1, wherein said TNF- α binding molecule further comprises a heavy chain variable region, wherein said heavy chain variable region comprises a human germline framework region.

9. A composition comprising a TNF- α binding, or a nucleic acid sequence encoding a TNF- α binding molecule, wherein said TNF- α binding molecule neutralizes human TNF- α cytotoxicity in an in vitro, cell-based assay with an EC₅₀ of 2.0 x 10⁻¹¹ or less.

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10. The composition of Claim 9, wherein said TNF- α binding molecule has a binding affinity (K_d) for human TNF- α of 7.5 x 10⁻¹² M or less.

11. The composition of Claim 9, wherein said TNF- α binding molecule has an 10 association rate (kon) for human TNF- α of 3.0 x 10⁶ M⁻¹ s⁻¹ or greater.

12. The composition of Claim 9, wherein said TNF- α binding molecule has a dissociation rate (koff) for human TNF- α of 1.0 x 10⁻⁴ s⁻¹ or less.

15 13. The composition of Claim 9, wherein said TNF- α binding molecule comprises a light chain variable region, wherein said light chain variable region comprises a human germline framework region.

20 14. The composition of Claim 9, wherein said TNF- α binding molecule comprises a heavy chain variable region, wherein said heavy chain variable region comprises a human germline framework region.

15. A method treating a TNF- α mediated disease comprising;

25 a) providing;

i) a subject, and

ii) a composition, wherein said composition comprises TNF- α binding molecules that neutralize human TNF- α cytotoxicity in an in vitro, cell-based assay with an EC₅₀ of 2.0 x 10⁻¹¹ or less; and

30 b) administering said composition to said subject.

16. The method of Claim 15, wherein said TNF- α mediated disease is selected from sepsis, an autoimmune disease, and rheumatoid arthritis.

17. The method of Claim 15, wherein said TNF- α binding molecules have a binding affinity (K_d) for human TNF- α of 7.5×10^{-12} M or less.

18. The method of Claim 15, wherein said TNF- α binding molecules have an 5 association rate (k_{on}) for human TNF- α of 3.0×10^6 M $^{-1}$ s $^{-1}$ or greater.

19. The method of Claim 15, wherein said TNF- α binding molecules have a disassociation rate (k_{off}) for human TNF α of 1.0×10^{-4} s $^{-1}$ or less.

10 20. The method of Claim 15, wherein said TNF- α binding molecule comprises a light chain variable region, wherein said light chain variable region comprises a human germline framework region.

15 21. The method of Claim 15, wherein said TNF- α binding molecule comprises a heavy chain variable region, wherein said heavy chain variable region comprises a human germline framework region.

20 22. A composition comprising a TNF- α binding molecule, or a nucleic acid sequence encoding a TNF- α binding molecule, wherein said TNF- α binding molecule comprises at least one of the following CDR sequences; i) a CDRL1 sequence comprising SEQ ID NO:93; ii) a CDRL2 sequence comprising SEQ ID NO:95; iii) a CDRL3 sequence comprising SEQ ID NO: 97; iv) a CDRH1 sequence comprising SEQ ID NO:87; v) a CDRH2 sequence comprising SEQ ID NO:89, and vi) a CDRH3 sequence comprising SEQ ID NO: 91.

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23. The composition of Claim 22, wherein said TNF- α binding molecule comprises at least three of said CDR sequences.

30 24. The composition of Claim 22, wherein said TNF- α binding molecule comprises all six of said CDR sequences.